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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 06/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/555,296	NUTTALL ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 20003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,18-34 and 39-51* is/are pending in the application.

4a) Of the above claim(s) *2,3,5,7-9 and 45-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,6,10,18-34 and 39-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-10,18-34 and 39-51* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/4/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of the species of amino acids for the first and second binding site of Figure 4 (SEQ ID NO: 4) in the communication of 19 November 2003 is acknowledged. Applicant's election without traverse of the histamine/serotonin binding compound of Figure 4, the type of histamine/serotonin binding compound, the type of peptide fusion, and the type of additional peptide in a composition in the communication of 04 April 2004 is acknowledged. However, because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 2-3, 5, 7-9, 45-51 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group or species, there being no allowable generic or linking claim. Election was made **without** traverse in the responses of 04 April 2003, 02 September 2003, and 19 November 2003. It is noted to Applicant that regarding the second binding site, amino acid residue 52 of SEQ ID NO: 4 for position III is not an aspartate. Also, amino acid residue 152 for position IV is not a glutamate. Therefore, claims 2-3 and 5 were considered non-elected.

Claims 1, 4, 6, 10, 18-34, and 39-44 are under consideration in the instant application as they read upon the elected species of a histamine or serotonin binding protein which has a first binding site and a second binding site; a histamine or serotonin binding compound which comprises a synthetic compound; a histamine or serotonin binding compound that is genetically fused to one or more peptides; cysteinyl leukotriene; SEQ ID NO: 4; the species of isoleucine at

position I, tryptophan at position II, aspartate at position III, and glutamate at position IV with regard to the first binding site; and the species of isoleucine at residue I, tryptophan at residue II, glycine at residue III, and aspartate at residue IV with regard to the second binding site.

Sequence Compliance

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). **Specifically, the nucleic acid sequences disclosed in Figures 1-11 and the amino acid sequences in Figure 22 are not accompanied by the required reference to the relevant sequence identifiers. Additionally, the specification discloses primer sequences at pages 22-23 and 25 that are not accompanied by the required reference to the relevant sequence identifiers.** This application fails to comply with the requirements of 37 CFR 1.821 through 1.825. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825).

Specification

2. The disclosure is objected to because of the following informalities:

3. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

4. Although the claims were amended to change the residue positions for SEQ ID NO: 4 in the amendment of 09 September 2003, the specification was not amended to include these changes.

Appropriate correction is required.

Claim Objections

5. Claims 1, 4, 6, 10, 18-21, 25-30, 32-34, and 39-44 are objected to because of the following informalities:

6. Claims 1, 4, 6, 27, 32 recite a non-elected groups and species.

7. Claims 6, 10, 18-21, 25-26, 28-30, 32-34, and 39-44 depend from claims 2, 3, and 51, which are currently withdrawn.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 1, 4, 6, 10, 18-34, and 39-44 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The claims read on a product of nature in that the claimed binding compound is not "isolated". In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty,* 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or "purified" as taught by pages pg 23-24 of the specification. See MPEP 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 4, 6, 10, 18-24, and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated histamine binding peptide capable of binding to histamine with a dissociation constant of less than 10^{-7}M which comprises the amino acid sequence of SEQ ID NO: 4 and has a binding site comprising amino acid residues isoleucine at position I, tryptophan at position II, aspartate at position III, and glutamate at position IV wherein residues I to IV are positioned at residues 139, 71, 67, and 112 in SEQ ID NO: 4, does not reasonably provide enablement for a histamine or serotonin binding compound capable of binding to histamine or serotonin with a dissociation constant of less than 10^{-7}M and which has a binding site comprising amino acid residues isoleucine at position I, tryptophan at position II, aspartate at position III, and glutamate at position IV wherein residues I to IV are positioned substantially the same as residues 139, 71, 67, and 112 in SEQ ID NO: 4, and functional equivalents thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to a histamine or serotonin binding compound capable of binding to histamine or serotonin with a dissociation constant of less than 10^{-7}M and which has a binding site comprising amino acid residues isoleucine at position I, tryptophan at position II, aspartate at position III, and glutamate at position IV wherein residues I to IV are positioned substantially the same as residues 139, 71, 67, and 112 in SEQ ID NO: 4, and functional equivalents thereof. The claims also recite that a histamine or serotonin binding compound additionally comprising at residue V, a tyrosine residue, wherein residue V is positioned substantially the same as residue 114 in SEQ ID NO: 4, and functional equivalents thereof. The claims recite that the compound

is stabilized by either or both disulphide bridges formed between cysteines 162 and 134 of SEQ ID NO: 4. Claim 10 recites that the histamine or serotonin binding compound comprises a synthetic compound. The claims also recite that the compound is produced by recombinant DNA technology, has a reporter molecule attached, is derived from blood-feeding ectoparasites, spiders, scorpions, or snakes and venomous animals, and is bound to a resin support.

The specification teaches that a functional equivalent means "compounds that possess the desired binding site and includes any macromolecule or molecular entity that binds to histamine or serotonin with a dissociation constant of 10^{-7}M or less and that possesses an equivalent complementarity of shape" (pg 6, lines 13-16). The specification also teaches that fragments is meant "any portion of the entire protein sequence that retains the ability to bind vasoactive amines with a dissociation constant of 10^{-7}M or less....Variants may include, for example, mutants containing amino acid substitutions, insertions or deletions from the wild type sequence of Figures 1 to 4" (pg 7, lines 12-18). However, the specification only teaches the binding *protein* comprising the amino acid sequence of SEQ ID NO: 4 and its characterization (pg 26-28). The specification does not teach any other histamine or serotonin *compounds* or functional equivalents. The specification does not teach functional or structural characteristics of all possible histamine or serotonin binding compounds in the context of a cell or organism. It is also noted that the specification only discloses that the D.RET6 protein of SEQ ID NO: 4 binds histamine (pg 27, lines 16-24; Figure 15). The specification only teaches that the binding of D.RET6 for histamine increases in the presence of serotonin (pg 27, lines 25-31; Figure 16). The specification does not indicate that serotonin binds the D.RET6 protein of SEQ ID NO: 4.

Furthermore, regarding functional equivalents of a protein, for example, the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding

residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

Due to the large quantity of experimentation necessary to generate the infinite number of histamine or serotonin binding compounds and their derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

10. Claims 25-28, 30-34, and 39-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a histamine or serotonin binding compound associated with one or more carbohydrate moieties or with one or more peptides or polypeptides. The claims

recite that the compound is attached to a toxin. The claims recite a therapeutic or diagnostic composition or a vaccine comprising a histamine or serotonin binding compound. The claims recite that the compound additionally comprises a cysteinyl leukotriene. The claims recite a compound for use in therapy; for use in the detection or quantification of histamine in human, animal, plant, and food material; for use in the depletion or removal of histamine from food products, cell cultures, or human, animal, plant, and food material; of r use in the binding or detection of histamine in humans and animals; for use an anti-histamine agent, an anti-inflammatory drug or in the treatment of allergy; for use as a toll in scientific research concerning the role of histamine in biological processes. The claims recite a method for treating or preventing inflammation or allergic reaction in humans or animals comprising administering a therapeutically effective amount of the histamine or serotonin binding compound.

The specification of the instant application teaches that a histamine or serotonin binding compound may include an additional protein or polypeptide to aid in the detection, expression of separation or purification of the protein or may be to lend additional properties to the protein as desired (pg 10, lines 26-30). The specification also discloses that histamine or serotonin binding compounds may be used as anti-inflammatory agents or may be used to bind histamine or serotonin in mammals, thereby to regulate their action and to control their pathological effects (pg 13, lines 19-21). The specification teaches that the histamine or serotonin binding compounds may be used as anti-inflammatory agents or agents to counter the effects of allergic reactions in the body (pg 13, lines 24-26). The specification also discloses numerous uses of the claimed histamine or serotonin binding compounds at pg 14-16. However, the specification does not teach any methods or working examples that indicate any histamine or serotonin binding

molecule is fused with a carbohydrate moiety or another protein. The specification also does not teach any methods or working examples to indicate that the claimed compound is joined with a toxin. Undue experimentation would be required of one skilled in the art to fuse all possible histamine/serotonin binding molecules with any carbohydrate, protein, or toxin and screen them for activity.

Additionally, the specification does not teach how to use a histamine or serotonin binding compound therapeutic composition without undue experimentation for the treatment of a condition or disease in an animal. The specification lists disorders and conditions to be treated (pg 14-16), but there are no working examples directed to a particular disorder in an animal or administration of the binding compound to an animal for treatment. (Note, this issue could be overcome by deleting the word "therapeutic" or "pharmaceutically-acceptable carrier" from the claims.)

Furthermore, the specification at pg 12-16 outlines prophetic procedures for administering a histamine or serotonin binding compound to a subject for the treatment of various conditions or disorders. There is also little or no guidance in the specification indicating the binding compound detects or quantifies histamine in animal, plant, food material; depletes or removes histamine from food products, cell culture, or animal, plant, food material; binds or detects histamine in humans or animals; or can be used as a tool in scientific research concerning the role of histamine. This is not adequate guidance, but is merely an invitation for the artisan to use the current invention as a starting point for further experimentation. For example, the prophetic examples do not teach the skilled artisan the optimal dosage, duration, and mode of administration of any histamine or serotonin binding compound. Furthermore, the claimed

method may not necessarily treat allergy or inflammation or remove histamine from food products, for example. The skilled artisan must resort to trial and error experimentation to determine the optimal dosage, duration, and mode of administration of all possible histamine and serotonin binding compounds. Such trial and error experimentation is considered undue. According to MPEP § 2164.06, "the guidance and ease in carrying out an assay to achieve the claimed objectives may be an issue to be considered in determining the quantity of experimentation needed." Also, the present invention is unpredictable and complex wherein one skilled in the art may not necessarily detect or quantify histamine in animal, plant, food material; deplete or remove histamine from food products, cell culture, or animal, plant, food material; or bind or detect histamine in humans or animals, for example, with a histamine or serotonin binding compound.

Regarding the use of the histamine or serotonin binding compound as a vaccine, the state of the art is such that numerous problems exist in regards to administering a subunit (antigen) vaccine to humans and animals. Several characteristics of an ideal vaccine, regardless of species, must include: 1) efficacy greater than 90%, 2) effective after a single dose, 3) long lived immunity, 4) effective when given orally, and 5) high safety (Babiuk, LA. *Vaccine 17*: 1587-1595, 1999). Often, when some proteins are included in a vaccine, they may be immunosuppressive, but in other cases, the immune responses to proteins may enhance the disease (Babiuk, pg 1588, col 2). Although antigen vaccines have the advantage of increased safety, their major disadvantages are their low level of immunogenicity and rapid degradation *in vivo*. The rapid degradation *in vivo* may explain the low immunogenicity, even if linked to a carrier or strong adjuvant (pg 1588, col 2; pg 1590, col 2).

Finally, the specification does not disclose preventing inflammation or allergic reaction by administration of a histamine or serotonin binding compound in any animal. The term "prevent" is interpreted as meaning that an activity will not occur, i.e. inflammation will not occur or allergic reaction will not occur. Undue experimentation would be required of the skilled artisan to determine the quantity of binding compound administered, the best route of administration, the duration of treatment, and any possible side-effects to prevent inflammation or allergic reaction.

Due to the large quantity of experimentation necessary to generate and screen histamine/serotonin binding compounds fused with carbohydrate moieties, proteins, or toxins for activity, to determine the quantity of histamine or serotonin binding compound to be administered, the most effective administration route, and the duration of the treatment, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of preventing inflammation or allergic reaction or the effects of the histamine or serotonin binding compound *in vivo,* undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

11. Claims 1, 4, 6, 10, 18-34, and 39-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification teaches that a functional equivalent means "compounds that possess the desired binding site and includes any macromolecule or molecular entity that binds to histamine or serotonin with a dissociation constant of 10^{-7}M or less and that possesses an equivalent complementarity of shape" (pg 6, lines 13-16). The specification also teaches that fragments is meant "any portion of the entire protein sequence that retains the ability to bind vasoactive amines with a dissociation constant of 10^{-7}M or less...Variants may include, for example, mutants containing amino acid substitutions, insertions or deletions from the wild type sequence of Figures 1 to 4" (pg 7, lines 12-18). However, the specification does not teach functional or structural characteristics of variants of SEQ ID NO:4 or all possible histamine or serotonin binding compounds capable of binding to histamine or serotonin with a dissociation constant of less than 10^{-7}M and which have a binding site comprising amino acid residues isoleucine at position I, tryptophan at position II, aspartate at position III, and glutamate at position IV wherein residues I to IV are positioned substantially the same as residues 139, 71, 67, and 112 in SEQ ID NO: 4 in the context of a cell or organism. The description of one D.RET6 polypeptide species (SEQ ID NO: 4) is not adequate written description of an entire genus of functionally equivalent compounds which incorporate all variants and fragments capable of binding to histamine or serotonin with a dissociation constant of less than 10^{-7}M and which have a binding site comprising amino acid residues isoleucine at position I, tryptophan at position II, aspartate at position III, and glutamate at position IV.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry,

whatever is now claimed" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the amino acid sequence of SEQ ID NO: 4, the skilled artisan cannot envision the detailed chemical structure of the encompassed compounds or polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, an isolated histamine and serotonin binding peptide capable of binding to histamine or serotonin with a dissociation constant of less than 10^{-7}M which comprises the amino acid sequence of SEQ ID NO: 4, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

35 USC § 112, second paragraph

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1, 4, 6, 10, 18-34, and 39-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. The term "substantially the same" in claims 1, 4, 6, 10, 18-34, and 39-44 is a relative term which renders the claims indefinite. (See claims 1 and 4-5, in particular.) The term "substantially the same" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Neither the specification nor the art provide unambiguous definitions for "the same" and "substantially the same" therefore, the metes and bounds of the claims cannot be determined by one skilled in the art.

15. Claim 4 is rejected as being indefinite because the nexus between the claim and the disclosed amino acid sequence of SEQ ID NO: 4 cannot be determined. For example, claim 4 recites that a tyrosine is positioned at residue 114 in SEQ ID NO: 4. However, a valine is actually positioned at residue 114 in SEQ ID NO: 4.

16. Claim 6 is rejected as being indefinite because the nexus between the claim and the disclosed amino acid sequence of SEQ ID NO: 4 cannot be determined. For example, claim 6 recites that cysteines are positioned at residues 162 and 134 of SEQ ID NO: 4. However, glycines are positioned at residues 162 and 134 in SEQ ID NO: 4.

17. The term "binds specifically" in claim 19 is a relative term which renders the claim indefinite. The term "binds specifically" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would

not be reasonably apprised of the scope of the invention. Neither the specification nor the art provide unambiguous definitions for "binds" and "binds specifically" therefore, the metes and bounds of the claims cannot be determined by one skilled in the art.

18. The term "effector molecule" in claim 20 is a relative term which renders the claim indefinite. The term "effector molecule" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear what molecules the claim encompasses. For example, is an "effector molecule" an enzyme, a radioactive label, a chemotherapeutic agent, etc. ?

19. The term "is associated with" in claims 25-27 is a relative term which renders the claims indefinite. The term "is associated with" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It cannot be determined if the binding compound binds the carbohydrate moieties/peptides or if the binding compound is fused to the moieties/peptides.

20. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely

exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 29 recites the broad recitation "a support", and the claim also recites "a resin" which is the narrower statement of the range/limitation.

21. Claims 34 and 39-43 provide for the use of a histamine or serotonin binding compound, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 34 and 39-43 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Double Patenting

22. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

23. Claims 1, 4, 19, 21-22, 24, 29-30, 33-34, 39, and 41-44 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,617,312. Although the conflicting claims are not identical, they are not patentably distinct from each other. The patented claims of a vasoactive amine binding protein having a sequence homology to a VABP clone, such as D.RET6 (SEQ ID NO: 22), and that contains a sequence motif consisting of (Asp or Glu)-Ala-Trp-(Lys or Arg) render obvious the pending claims reciting a histamine or serotonin binding molecule with a dissociation constant of less than 10^{-7}M and which has a binding site comprising amino acid residue isoleucine at position I, tryptophan at position II, aspartate as position III, and glutamate at position IV, wherein residues I to V are positioned substantially the same as residues 139, 71, 67, and 112 in SEQ ID NO: 4. Specifically, the pending claims recite molecules that overlap with the patented genus claims. The specification of the instant application and the '312 patent teach that vasoactive amines include histamine and serotonin (see instant specification pg 1, line 11; '312 patent, col l 1, line 23). Furthermore, the amino acid positions recited in the instant claims are the same positions in the D.RET6 amino acid sequence in the '312 patent. Also, SEQ ID NO: 4 of the instant application contains a sequence motif consisting of (Asp or Glu)-Ala-Trp-(Lys or Arg) (see amino acids 44-47 of SEQ ID NO: 4, for example). Therefore, the instant claims are not patentably distinct over the issued claims in U.S. patent 6,617,312.

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Paesen et al. Biochim Biophys Acta. 1309(1-2):9-13, 1996.

Paesen et al. Biochim Biophys Acta. Oct 18;1482(1-2):92-101, 2000.

Paesen et al. Mol Cell. 3(5):661-71, 1999.

Sangamnatdej et al. Insect Molec Biol 11(1) : 79-86, 2002.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

BEB
Art Unit 1647
07 June 2004

ELIZABETH KEMMERER
PRIMARY EXAMINER